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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
ISABELLA, DAVID J	

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3774	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/782,750	VACANTI ET AL.	
	Examiner	Art Unit	
	DAVID J. ISABELLA	3774	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 February 2007*.

2a)☒ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5 and 8-17* is/are pending in the application.

4a) Of the above claim(s) *16 and 17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,8-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Response to Arguments

Applicant's arguments filed 5/8/2007 have been fully considered but they are not persuasive.

Applicant argues that Mikos in view of Sparks or Jauregui fails to disclose or suggest a method for making a cell matrix construct that is to be used as a heart valve. The method includes forming a biodegradable polymer matrix in a shape of a heart valve/leaflet, seeding the matrix with cells and forming a construct that can withstand repeated stress and strain.

Applicant further argues that Sparks does not teaçh or suggest that the use of a bio-degradable polymer matrix that is seeded with cells. Sparks discloses various methods for populating and growing new tissues including seeding, pre-clotting the matrix with blood and natural induction of tissue growth into the matrix. Beyond Sparks, it was certainly known at the time of applicant's invention to pre-seed polymer matrix prior to implanting the matrix in the body for growing new tissue. Applicant's attention is directed to Mikos specification, in the background of the invention, Vacanti's teachings for pre-seeding polymer matrixes prior to implantation to optimize new tissue formation and growth.

Examiner believes that *prima facie* case of obviousness has been properly established in that there are sufficient suggestions/motivation to modify or combine the references to suggest the claimed limitations. Such modifications were made with a reasonable expectation of success.The level of one of ordinary skilled in the art is

extraordinarily high typically requiring MD, Phd and post-docorate degrees. Examiner has outlined the differences between the prior art and the claims at issue.

Claims were rejected as being unpatentable over Mikos as modified by Sparks or Jaurequi. Mikos, the primary reference, lacks the specific teachings of forming a vascular tissue equivalent e.g. heart valve or heart valve leaflet. The secondary references were applied to teach the forming of vascular tissue equivalent e.g. heart valve or heart valve leaflet using a template seeded with specialized cells.

Claims were rejected as being unpatentable over Sparks in view of Mikos or Griffith-Cima et al. Sparks, the primary reference, lacks the specific teachings using a biodegradable template for the reinforcing mesh upon which to grow new vascularized tissues. Secondary references to Mikos and Griffith-Cima et al teaches seeding bio-degradable material with specialized cells for growing new tissues upon a degradable template. Examiner has answered applicant's arguments in the body of the rejection.

Status of the Claims

Claims 1-5,8-17 are currently pending for action. Claims 6 and 7 have been cancelled. Claims 16 and 17 stand withdrawn from consideration as these claims are directed to an invention that is independent or distinct from the invention originally claimed. The original claims were directed to a method for making a cell matrix construct including implanting the construct into an animal. No amendments were made to the claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-5,8-11,15/1,15/2,15/3,15/4,15/5,15/8,15/9,15/10,15/11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mikos (5514378) in view of Sparks (3514791) or Jauregui (4795459).

Claim 1 does not require matrix to be first cultured at a first in vivo site prior to being transplanted to a second site. Therefor, the claim is directed to a method for making a cell-matrix construct comprising implanting into an animal a biodegradable polymer construct in the shape of a heart valve or valve leaflet. The construct having seeded cells therein. The cells may be endothelial, myofibroblast, skeletal muscle, vascular smooth muscle, myocytes, fibromyoblast, and ectoderamal in source.

Mikos discloses every element/step of the claim except for the disclosure of the matrix to be in the form of a heart valve or valve leaflet. In column 1, the background of the invention, Mikos identifies that cells cannot form new tissues on their own but require supporting material to act as a template for growth.

> Isolated cells cannot form new tissues on their own. Most cells have a requirement for attachment to a surface in order to replicate and function. They require specific environments which very often include the presence of supporting material to act as a template for growth. Three dimensional scaffolds are used to mimic their natural counterparts, the extracellular matrices of the body. They serve as both a physical support and an adhesive substrate for isolated parenchymal cells during "in vitro" culture and subsequent implantation.

Mikos, column 2, lines 15+, discloses an article by Vacanti, et al (1988) teaching that the scaffold should mimic the natural tissue counterpart. Moreover, Vacanti, et al states that the scaffold should serve as both a physical support and an adhesive substrate for isolated cells during the culturing thereof.

Vacanti, et al., "Selective cell transplantation using bioabsorbable artificial polymers as matrices" *J. Pediat. Surg.* 23, 3–9 (1988) and Vacanti, "Beyond Transplantation" *Arch. Surg.* 123, 545–549 (1988), describe an approach for making new organs for transplantation which was not subject to the same limitations as the work of Yannas and Burke, i.e., it was not limited to the construction of very thin organs such as skin. Vacanti, et al., recognized that cells require a matrix for attachment and support if they are to survive following implantation, that a minimum number of cells was essential for function in vivo, and that the matrix must be porous enough to allow nutrients and gases to reach all of the cells on and within the matrix by diffusion, until the matrix-cell structure was vascularized. Moreover, they recognized the advantage of using synthetic biodegradable polymer substrates to form a scaffold that mimics its natural counterparts, the extracellular matrices (ECM) of the body, serving as both a physical support and an adhesive substrate for isolated parenchymal cells during in vitro culture, and subsequent implantation, degrading as the cells begin to secrete they own ECM support. Subsequent studies have demonstrated that even better results are obtained when the matrix is first implanted, prevascularized, and then seeded with cells. Most matrices used in the earlier work are modifications of materials already available, such as surgical sutures and meshes. This latter approach, however, requires new matrix configurations which are optimal for vascularization, yet resistant to compression, with sufficient porosity and interconnected interstitial spacings to allow injected cells to become dispersed throughout the matrix.

Furthermore, Mikos is specific as to the purpose of tailoring the bioabsorbable matrix according to the selected biological tissue to be grown. See column 13, lines 31+.

The matrix scaffold is used to mimic its natural counterparts, the extracellular matrices (ECM) of the body. It serves as both a physical support and an adhesive substrate for isolated parenchymal cells during in vitro culture and subsequent implantation. As the transplanted cell population grows and the cells function normally, they begin to secrete their own ECM support. Concurrently, when using a biodegradable matrix material, the scaffold continuously degrades and is eliminated as the need for an artificial support diminishes. In the reconstruction of structural tissues like cartilage and bone, tissue shape is integral to function. Therefore, these scaffolds must be processable into devices of varying thickness and shape.

Preparation of Anatomical Shapes

The membranes are processed into anatomical shapes, or foams, for use in reconstructive surgery or organ transplantation, as depicted in FIG. 3 (described in more detail

Contrary to applicant's argument that Mikos fails to disclose matrices having the desired function of the particular tissue, in column 4, lines 49-54, Mikos discloses that the advantages of using membranes that may be assembled in a desired shape is that polymers with different properties and different porosities can be used to assemble the scaffold as it occurs in nature.

> The three dimensional structures are formed by layering the membranes until a laminated structure is assembled in a desired shape. A particular advantage of the use of the membranes is that polymers with different properties, and membranes with different porosities, can be used to assemble the structure, much as occurs in nature.

Moreover, Mikos teaches that various cells types may be used for culturing new tissues. See column 14, lines 25+.

> Use of the Matrix for Reconstructive Surgery
>
> The three-dimensional structure is specifically designed to provide a matrix for dissociated cells such as chondrocytes or hepatocytes to create a three-dimensional tissue or organ. Any type of cell can be added to the matrix for culturing and possible implantation, including cells of the muscular and skeletal systems, such as chondrocytes, fibroblasts, muscle cells and osteocytes, parenchymal cells such as hepatocytes, pancreatic cells (including Islet cells), cells of intestinal origin, and other cells such as nerve cells and skin cells, either as obtained from donors, from established cell culture lines, or even before or after genetic engineering. Pieces of tissue can also be used, which may provide a number of different cells types in the same structure.
>
> The cells are obtained from a suitable donor or the patient into which they are to be implanted, dissociated using standard techniques, and seeded onto and into the matrix. These are optionally cultured in vitro prior to implantation. Alternatively, the matrix is implanted, allowed to vascularize, then the cells injected into the matrix. Methods and reagents for culturing cells in vitro and implantation of a matrix are known to those skilled in the art.

Each of Jauregui and Sparks teaches the seeding of a scaffold with tissues/cells for growing heart valve/leaflets. While Mikos is silent to growing of vascular tissues, the use of tissue engineering employing both bioresorbable and nonresorbable polymer scaffolds to replace diseased, defective or injured tissues, including vascular tissues, is

known in the art as taught by Jauregui and Sparks. In column 1, lines 10-40 of Jauregui, Jauregui teaches that cells have been seeded on devices to promote endothelialization

It may be desirable to provide a layer of cells on a surface of an implanted prosthetic device. E.g., implantable cardiovascular devices, e.g., vascular prostheses, artificial hearts, and heart valves, should support rapid endothelial coverage and allow a maximal rate of endothelial migration on their surfaces, because incomplete endothelialization of such surfaces may eventually lead to thrombo-embolic episodes and ultimately to failure of some of these prosthetic devices.

Endothelial cells have been seeded on prosthetic devices to promote endothelialization, as is discussed in Bourke, M. et al., "Endothelial cell harvest for seeding vascular prostheses: The influence of technique on cell function, viability, and number," *J. Vascular Surgery*, Vol. 4, No. 3, Sept. 1986, pp. 257–263. Jarrell et al., "Use of Endothelial Monolayer on a Vascular Graft Prior to Implantation", *Ann. Surg.*, June 1986, pp. 671–678, and Jarrell et al., "Use of Freshly Isolated Capillary Endothelial Cells for the Immediate Establishment of a Monolayer on a Vascular Graft at Surgery", *Surgery*, Vol. 100, No. 2, August 1986, pp. 392–399, describe the desirability of establishment of an intact endothelium at or near time of implantation, and seeding of endothelial cells on a woven Dacron surface pretreated with platelet rich plasma or human amnion. Fasol, R. et al., "Experimental In Vitro Cultivation of Human Endothelial Cells on Artificial Surfaces", *Trans. Am. Soc. Artif. Intern. Organs*, Vol. XXXI, 1985, pp. 276–283, discloses treating PTFE with fibronectin to promote growth of an endothelial layer thereon.

. Sparks teaches seeding scaffolds with tissues/cells for growing vascular tissues. Examiner maintains that all the elements were known in the prior art and that though Mikos preferred embodiment is directed to bone/cartilage, one skilled in the art could have looked to the teachings of either of Jauregui or Sparks and could have combined the elements/steps as claimed by known methods with no change in their repsective functions, and the combination would have yielded predictable results at the time of the invention. Therefor, the method of Mikos in producing a vascular tissue equivalent using bioresorbable scaffold seeded with tissues/cells would have been

obvious to one with ordinary skill in the art from the teachings of either of Jauregui or Sparks.

With respect to applicant's assertion that Mikos as modified by the teachings of Jauregui or Sparks would result in avascular tissue is not well taken since the secondary teachings are primarily concerned with vascularized scaffolding. Claim 1 recites "construct can withstand repeated stress and strain". While applicant argues that the replacement valve or heart leaflet structure must open and close hundreds of times every hour, thousands of times every day, for years, such interpretation is not commensurate with the scope of the claim. Moreover, the resulting tissue produced by Mikos, as modified, is designed to be a tissue counterpart to be used in the heart as a valve or portion thereof and would reasonable have the structure and function of its tissue counterpart. Such tissue would possess the properties of elasticity, flexibility and strength corresponding to the native tissue.

Claim 2, see column 14, lines 25+ of Mikos.

Claim 3, see method of Sparks. Sparks teaches culturing a tissue replacement in vivo at a first site and removing the tissue replacement and transplanting the tissue replacement at a second site.

Claim 4, see teachings of Jauregui or Sparks for forming a scaffold in the form of a heart valve or valve leaftlet .

Claim 5, see column 14, lines 25 of Mikos.

Claim 8, since the tissue equivalent of Jauregui and Sparks are used to replace similar in vivo tissue, the tissue equivalent would inherently possess the require physical characteristics to perform the intended replacement function.

Claims 9 and 10, see column 3, lines 5+ of Mikos.

Claim 11, see graphs 2A&B of Mikos.

Claims 12-14,15/12,15/13,15/14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mikos (5514378) in view of Sparks (3514791) or Jauregui (4795459) further in view of Griffith-Cima et al (5709854).

The use of growth factors in combination with seeding of cells on a scaffold to promote cellular attachment and differentiation would have been obvious to one with ordinary skill in the art from the teachings of Griffith-Cima.

> The polymeric matrix can be combined with humoral factors to promote cell transplantation and engraftment. For example, the polymeric matrix can be combined with angiogenic factors, antibiotics, antiinflammatories, growth factors, compounds which induce differentiation, and other factors which are known to those skilled in the art of cell culture.
>
> For example, humoral factors could be mixed in a slow-release form with the cell-alginate suspension prior to formation of implant or transplantation. Alternatively, the hydrogel could be modified to bind humoral factors or signal recognition sequences prior to combination with isolated cell suspension.

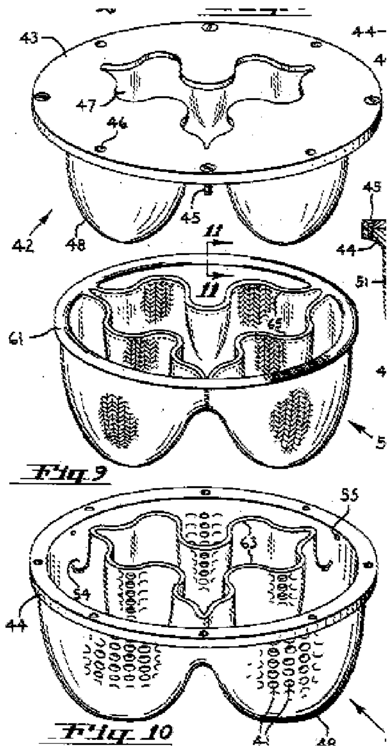
Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-5,8-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sparks (3514791) in view of Mikos (5514378) or Griffith-Cima et al (5709854) and in view of the teachings of either of Jauregui (4795459) or Tang et al (4916193).

Sparks discloses a method for making a cell-matrix construct for use as a heart valve comprising implanting into an animal a fibrous matrix formed of a polymer that has been seeded with specific selected cells. Contrary to applicant's arguments that Sparkes fails to disclose the use of a fibrous polymeric matrix in the shape of a heart valve or leaflet, applicant attention is directed to column 5,lines 5-75 for the specific disclosure directed to the method for forming any of a tricuspid, bicuspid or individual valve leaflets. Figure 10, illustrates one embodiment for a die used in manufacturing a tricuspid valve.



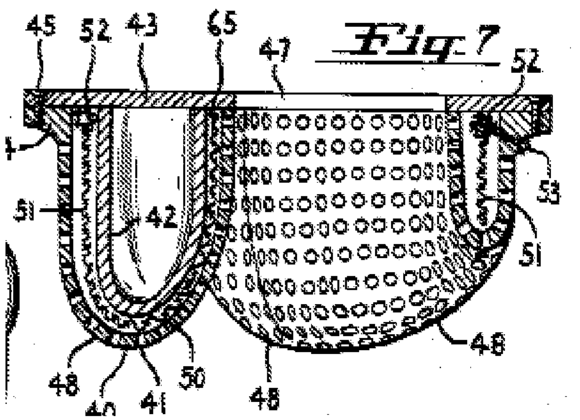


Figure 7, shows reinforcing mesh 51 approximating the shape of the die forming the leaflets. Column 5, lines 32-36 and 55-60, Sparks clearly teaches that the mesh has the same configuration as the die cavity.

Applicant argues that Sparks discloses a stainless steel die that is reinforced with a non-biodegradable reinforcing mesh. Examiner reminds applicant that the claim

is directed to a method which utilizes the transition phrase “comprising” and this allows for other elements and/or steps not specifically set forth in applicant’s claims (i.e. stainless steel die). Sparks fails to teach that the matrix is biodegradable. Mikos and Griffith-Cima et al teach the use of biodegradable matrix which is designed to allow biological tissue ingrowth to form a structure before the matrix is completely bioabsorbed.

Mikos, column 2, lines 15+, discloses an article by Vacanti, et al (1988) teaching that the scaffold should mimic the natural tissue counterpart. Moreover, Vacanti, et al provides evidence that better results are obtained when the matrix is first implanted, prevascularized and then seeded with select cells.

> Vacanti, et al., "Selective cell transplantation using bioabsorbable artificial polymers as matrices" *J. Pediat. Surg.* 23, 3–9 (1988) and Vacanti, "Beyond Transplantation" *Arch. Surg.* 123, 545–549 (1988), describe an approach for making new organs for transplantation which was not subject to the same limitations as the work of Yannas and Burke, i.e., it was not limited to the construction of very thin organs such as skin. Vacanti, et al., recognized that cells require a matrix for attachment and support if they are to survive following implantation, that a minimum number of cells was essential for function in vivo, and that the matrix must be porous enough to allow nutrients and gases to reach all of the cells on and within the matrix by diffusion, until the matrix-cell structure was vascularized. Moreover, they recognized the advantage of using synthetic biodegradable polymer substrates to form a scaffold that mimics its natural counterparts, the extracellular matrices (ECM) of the body, serving as both a physical support and an adhesive substrate for isolated parenchymal cells during in vitro culture, and subsequent implantation, degrading as the cells begin to secrete they own ECM support. Subsequent studies have demonstrated that even better results are obtained when the matrix is first implanted, prevascularized, and then seeded with cells. Most matrices used in the earlier work are modifications of materials already available, such as surgical sutures and meshes. This latter approach, however, requires new matrix configurations which are optimal for vascularization, yet resistant to compression, with sufficient porosity and interconnected interstitial spacings to allow injected cells to become dispersed throughout the matrix.

Furthermore, Mikos is specific as to the purpose of tailoring the bioabsorbable matrix according to the selected biological tissue to be grown. See column 13, lines 31+.

> The matrix scaffold is used to mimic its natural counterparts, the extracellular matrices (ECM) of the body. It serves as both a physical support and an adhesive substrate for isolated parenchymal cells during in vitro culture and subsequent implantation. As the transplanted cell population grows and the cells function normally, they begin to secrete their own ECM support. Concurrently, when using a biodegradable matrix material, the scaffold continuously degrades and is eliminated as the need for an artificial support diminishes. In the reconstruction of structural tissues like cartilage and bone, tissue shape is integral to function. Therefore, these scaffolds must be processable into devices of varying thickness and shape.
>
> Preparation of Anatomical Shapes
>
> The membranes are processed into anatomical shapes, or foams, for use in reconstructive surgery or organ transplantation, as depicted in FIG. 3 (described in more detail

Moreover, Mikos teaches that various cells types may be used for culturing new tissues. See column 14, lines 25+.

> Use of the Matrix for Reconstructive Surgery
>
> The three-dimensional structure is specifically designed to provide a matrix for dissociated cells such as chondrocytes or hepatocytes to create a three-dimensional tissue or organ. Any type of cell can be added to the matrix for culturing and possible implantation, including cells of the muscular and skeletal systems, such as chondrocytes, fibroblasts, muscle cells and osteocytes, parenchymal cells such as hepatocytes, pancreatic cells (including Islet cells), cells of intestinal origin, and other cells such as nerve cells and skin cells, either as obtained from donors, from established cell culture lines, or even before or after genetic engineering. Pieces of tissue can also be used, which may provide a number of different cells types in the same structure.
>
> The cells are obtained from a suitable donor or the patient into which they are to be implanted, dissociated using standard techniques, and seeded onto and into the matrix. These are optionally cultured in vitro prior to implantation. Alternatively, the matrix is implanted, allowed to vascularize, then the cells injected into the matrix. Methods and reagents for culturing cells in vitro and implantation of a matrix are known to those skilled in the art.

Griffith-Cima teaches that the degradable template may be shaped or formed prior to implantation into the patient.

the hydrogel. However, the matrix may also be molded and implanted in one or more different areas of the body to suit a particular application. This application is particularly relevant where a specific structural design is desired or where the area into which the cells are to be implanted lacks specific structure or support to facilitate growth and proliferation of the cells.

The site, or sites, where cells are to be implanted is determined based on individual need, as is the requisite number of cells. For cells having organ function, for example, hepatocytes or islet cells, the mixture can be injected into the mesentery, subcutaneous tissue, retroperitoneum, properitoneal space, and intramuscular space. For formation of cartilage, the cells are injected into the site where cartilage formation is desired. One could also apply an external mold to shape the injected solution. Additionally, by controlling the rate of polymerization, it is possible to mold the cell-hydrogel injected implant like one would mold clay.

Alternatively, the mixture can be injected into a mold, the hydrogel allowed to harden, then the material implanted.

Each of Jauregui and Tang et al teaches the doctrine of equivalence between resorbable and non resorbable materials as used in heart valve applications similar to that as disclosed in column 4 of applicants specification. To replace the non-absorbable mesh of Sparks with an absorbable matrix as taught by Mikos or Griffith-Cima et al to allow for a degradable template for new tissue formation would have been obvious to one with ordinary skill in the art especially in light of the Vacanti publication (as disclosed in Mikos) which teaches the benefits of selected cells transplantation on bioabsorbable polymer matrix.

Applicant specification fails to teach and/or disclose any unobvious benefits or criticalities in the selection of the materials used for the seeding of the cells. Accordingly, examiner maintains that the materials used are well known in the art and are, in many instances, known equivalents as taught by Jauregui or Tang et al. It should be evident that at the time of Sparks invention (1967) the use of resorbable material in tissue applications was in its infancy. At the time of applicant's invention

(2004), great strides have been made in the prosthetic art in replacing non-resorbable materials with resorbable materials for various known benefits. The use of resorbable material as the substrate for seeding cells to form a tissue construct would have been obvious to one with ordinary skill in the art from the teachings of any of the secondary references. Examiner maintains that all the elements were known in the prior art and that though Sparks discloses non-biodegradable reinforcing mesh, one skilled in the art could have looked to the teachings of either of Mikos or Griffith-Cima et al to use biodegradable reinforcing mesh in place of the non-biodegradable mesh as claimed by known methods with no change in their repsective functions, and the combination would have yielded predictable results at the time of the invention.

With respect to the limitation of “withstand repeated stress and strain”, the device of Sparks as modified would inherently possess the properties that would be capable of withstanding cyclic stresses and strains since the valve is designed to function as a replacement of a natural existing valve. Applicant argues that the issue is “not merely using biodegradable materials to make heart valves and that biodegradable materials can be used in tissue engineering is known in the art, as correctly stated by the Examiner. It is also known that these polymers can be molded to mimic the shape of the tissue to be engineered. However, making a structure with the requisite mechanical physical and mechanical properties necessary for biological function has been the challenge”. Sparks tissue equivalent is designed for use as a replacement for the natural existing valve and would therefor inherently possess physical properties to perform the function of the natural valve. In replacing the non-biodegradable mesh of Sparks with a biodegradable mesh would eventually produce a tissue replacement having only natural confluent cells

in the form of vascularized tissue essentially an equivalent counterpart to the natural tissue of the heart. It is a reasonable expectation that the tissue equivalent would possess the structure and function of its tissue counterpart. Such tissue would possess the properties of elasticity, flexibility and strength corresponding to the native tissue.

Moreover, applicant specification discloses known materials and seeding methods used in producing tissue equivalents. Additionally, applicant's specification fails to particularly set forth specific unknown materials or modification thereof along with unique and/or unknown method steps to obtain a unique tissue equivalent. Applicant’s specification serves to further evidences that the steps of seeding a biodegradable template having a form of a portion of a heart leaflet or a heart valve with admitted known materials and methods as taught in the prior art would have yielded a reasonable expectation of success.

Claim 2, see cells disclosed by Sparks.

Claim 3, Sparks discloses the steps of culturing a matrix at a first site then transplanting the new tissue to a desired site.

Claim 4, one embodiment disclosed by Sparks is a heart valve.

Claim 5, see cells of sparks or Schmidt, et al.

Claim 8, the newly formed heart tissue of Sparks would inherently possess the strength, flexibility and/or pliability of the tissue it is to replace.

Claims 9 and 10, see materials disclosed by Mikos or Griffith-Cima et al.

Claim 11, see Mikos.

Claims 12-14, see Mikos or Griffith-Cima et al.

Claim 15, see construct of Sparks as modified by either of Mikos or Griffith-Cima et al.

Conclusion

, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to DAVID J. ISABELLA whose telephone number is 571-272-4749. The examiner can normally be reached on MONDAY-FRIDAY.

The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/DAVID J ISABELLA/
Supervisory Patent Examiner,
Art Unit 3774

DJI